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USSN 09/877,987 Filed: June 8, 2001

Dkt: D009NP;30436.53USU1

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In the Specification

Please replace the paragraph on page 9 beginning at line 23 and ending at line 29 with the following:

s of

*CTLA4Ig" is a soluble fusion protein comprising an extracellular domain of wild type CTLA4, or a portion thereof that binds a B7, joined to an Ig tail. A particular embodiment comprises the extracellular domain of wild type CTLA4 starting at methionine at position +1 and ending at aspartic acid at position +124; or starting at alanine at position -1 to aspartic acid at position +124; a junction amino acid residue glutamine at position +125; and an immunoglobulin portion encompassing glutamic acid at position +126 through lysine at position +357 (Figure 5 and SEQ ID NO:7). \$\P\$

Please replace the paragraph on page 12 beginning at line 2 and ending at line 7 with the following:



As used herein "the extracellular domain of CTLA4" is any portion of CTLA4 that recognizes and binds a B7. For example, an extracellular domain of CTLA4 comprises methionine at position +1 to aspartic acid at position +124 (Figure 5 and SEQ ID NO: 7). Alternatively, an extracellular domain of CTLA4 comprises alanine at position -1 to aspartic acid at position +124 (Figure 5 and SEQ ID NO: 7). The extracellular domain includes fragments or derivatives of CTLA4 that bind a B7.

Please replace the paragraph on page 15 beginning at line 15 and ending at line 29 with the following:



The first agent preferably acts by interfering with the interaction between a receptor on a lymphocyte (e.g., CD28 and/or CTLA4) and its ligand (e.g., B7-1 and/or B7-2). Examples of

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the first agent include, but are not limited to, molecules such as an antibody (or portion or derivative thereof) that recognizes and binds to the receptor or the ligand; a soluble form (or portion or derivative thereof) of the receptor or the ligand such as soluble CTLA4; a peptide fragment or other small molecule designed to interfere with the lymphocytic signal through the receptor/ligand mediated interaction. In a preferred embodiment, the first agent is a soluble CTLA4 molecule, such as CTLA4Ig (ATCC 68629) or L104EA29YIg (ATCC PTA2104), a soluble CD28 molecule such as CD28Ig (ATCC 68628), a soluble B7 molecule such as B7Ig (ATCC 68627), an anti-B7 monoclonal antibody (e.g. ATCC HB-253, ATCC CRL-2223, ATCC CRL-2226, ATCC HB-301, ATCC HB-11341 and monoclonal antibodies as described in references 80-81), an anti-CTLA4 monclonal antibody (e.g. ATCC HB-304, and monoclonal antibodies as described in references 82-83) and/or an anti-CD28 monoclonal antibody (e.g. mAb 9.3 as described in reference 79). American Type Culture Collection (ATCC) is located at 10801 University Blvd., Manasas, VA 20110-2209.

Please replace the paragraphs on page 16 beginning at line 1 and ending at line 27 with the following:

The second agent acts by interfering with the interaction between a second receptor on a lymphocyte (e.g., CD154) and its ligand (e.g., CD40). Examples of the second agent include, but are not limited to, molecules such as an antibody (or portion or derivative thereof) that recognize and bind the second receptor or the ligand such as an anti-CD154 monoclonal antibody; a soluble form (or portion or derivative thereof) of the receptor or the ligand; a peptide fragment or other small molecule designed to interfere with the lymphocytic signal through the second receptor/ligand mediated interaction. In a preferred embodiment, the second agent is an anti-CD154 (e.g. MR1 as described in reference 56, ATCC HB-10916, ATCC HB-12055 and ATCC HB-12056) and/or anti-CD40 monoclonal antibody (e.g. ATCC HB-9110). American Type Culture Collection (ATCC) is located at 10801 University Blvd., Manasas, VA 20110-2209.

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The third agent interferes with adhesion molecule (e.g. LFA-1) interactions with its ligands. Examples of adhesion molecules and ligands include, but are not limited to, LFA-1 (CD11a/CD18), Mac-1 (CD11b/CD18), p150,95 (CD11c/CD18), ICAM (1, 2 and 3), VLA-1, CD44, CD62 (E, L and P), CD106, fibrinogen, α-actinin, filamin and cytohesin-1. LFA-1 ligands such as ICAM-1, ICAM-2, ICAM-3, \alpha-actinin, filamin and cytohesin-1, etc., can be located on another cell or in the extracellular matrix. Examples of the third agent include, but are not limited to: molecules such as an antibody (or portion or derivative thereof) that recognizes and binds adhesion molecules or its ligands; a soluble form (or portion or derivative thereof) of the adhesion molecule or its ligand; a peptide fragment or other small molecule designed to interfere with the adhesion molecule/ligand interaction. In a preferred embodiment, the third agent is an anti-LFA-1 (e.g. ATCC HB-9579, and ATCC TIB-213), anti-ICAM-1 (e.g. ATCC CRL-1878 and ATCC HB-233), anti-ICAM-2, anti-ICAM-3, antiα-actinin (e.g. ATCC CRL-2252), anti-filamin, anti-cytohesin-1, anti-CD11a (e.g. M17/5.2 ATCC TIB-237, ATCC HB-202, ATCC HB-244, and ATCC TIB-217) and/or anti-CD18 (ATCC HB-203, ATCC HB-226 and ATCC TIB-218) monoclonal antibody. American Type Culture Collection (ATCC) is located at 10801 University Blvd., Manasas, VA 20110-2209.

Please replace the paragraph on page 30 beginning at line 4 and ending at line 6 with the following:

DNA encoding the amino acid sequences corresponding to B7Ig, CD28Ig and CTLA4Ig has been deposited with the American Type Culture Collection (ATCC), 10801 University Blvd., Manasas, VA 20110-2209, under the Budapest Treaty on May 31, 1991, and has been accorded ATCC accession numbers 68627, 68628 and 68629, respectively. DNA encoding the amino acid sequence corresponding to L104EA29YIg has been deposited with the ATCC under the Budapest Treaty on June 19, 2000, and has been accorded ATCC accession number

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